REMARKS

The present amendment under 37 CFR § 1.114 is in response to the Final Office Action dated April 16, 2002 and the Advisory Action dated December 15, 2003, and further to the Notice of Appeal filed on October 16, 2003. The Advisory Action alleges that Applicants' amendment under 37 CFR § 1.116 filed August 14, 2003, was non compliant for not listing withdrawn claims. All withdrawn claims are hereby canceled. The specification has been amended to add a statement regarding federally sponsored research. No new matter has been added. Claims 104, 105, and 107-112 are pending in this case. With the above amendment, claims 10, 23-103 and 105 has been canceled and claims 104, 107, and 109-111 have been amended for purposes of clarity and to advance prosecution of this application. It is urged that support for the above amendments can be found throughout the specification as originally filed and that none of the amendments constitutes new matter. In particular, support for compositions comprising immunogenic portions of WT1 can be found, for example, at page 9, line 27-page 10, line 2. It should also be noted that the above amendments are not to be construed as acquiescence with regard to the Examiner's rejections and are made without prejudice to prosecution of any subject matter modified and/or removed in a related divisional, continuation and/or continuation-in-part application.

Rejection under 35 U.S.C. § 112, first paragraph (written description)

Claims 104, 105, 110-112 stand rejected under 35 U.S.C. § 112, first paragraph as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor had possession of the claimed invention at the time the application was filed. In particular, the Action maintains that that there is no disclosure in the specification as to what amino acids would be altered to permit the claimed variant peptides to retain their ability to bind to MHC alleles. Therefore, the written description is allegedly not commensurate with the scope of the claimed invention.

Applicants respectfully traverse this rejection for the reasons already on record. In short, extensive discussion of variants of the present invention can be found, for example, from page 12, line 28 to page 14, line 8, and elsewhere. This includes a description of variants

containing between 1 and 3 amino acid substitutions, and includes a description that variants of the invention retain reactivity with antigen specific T-cell lines or clones. As discussed in Applicants' response to the Office Action dated April 23, 2001, filed October 23, 2001, Applicants submit that the skilled artisan would readily understand, in light of the applicants' disclosure, the single identifying characteristic common to the claimed variants, *i.e.*, their ability to stimulate T cells specific for SEQ ID NO:2, and would further appreciate the routine nature of the techniques used in their identification. Thus, in view of the applicants specification, and the routine and art recognized approaches for the identification and evaluation of variants that are reactive with antigen-specific T-cells, the person of ordinary skill in the art would recognize that the applicants were indeed in possession of the presently claimed invention as of the filing date of the captioned application. Nevertheless, solely in order to advance prosecution, Applicants have amended claims 104 and 110, without prejudice, to remove recitation of variants. Accordingly, Applicants submit that the rejection has been obviated and may be properly withdrawn.

Rejection under 35 U.S.C. § 112, first paragraph (new matter)

Claims 104, 105, 110-112 stand rejected under 35 U.S.C. § 112, first paragraph as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor had possession of the claimed invention at the time the application was filed. In particular, the Action opines that there is no support in the specification as filed for the recitation of "composition" in claims 108-112. The Action contends that the specification only discloses vaccines with "non-specific immune response enhancer" and therefore there is no support in the specification for the scope of "composition" recited in these claims. Accordingly, the Action concludes that the claimed invention constitutes new matter.

Applicants respectfully traverse this rejection and submit that the courts have held that all that is required to comply with the written description requirement is that the specification **reasonably convey** to persons skilled in the art that the inventor had possession of the subject matter claimed. (In re Edwards, 568 F.2d 1349, 1351, 196 USPQ 465, 467 (CCPA

1978) (emphasis added). Applicants submit that the specification as filed clearly describes compositions comprising WT1, for example, on page 9, line 25-page 10, line 2, as follows:

> **The compositions** described herein **may include WT1 polypeptides**, WT1 polynucleotides, antigen-presenting cells (APC, *e.g.*, dendritic cells) that express a WT1 polypeptide, agents such as antibodies that bind to a WT1 polypeptide and/or immune system cells (*e.g.*, T cells) specific for WT1. (emphasis added)

The specification goes on to describe certain preferred embodiments of compositions, *e.g.*, vaccines, in the context of the present invention on page 28, lines 10 - 18 as follows:

> **Within certain aspects, polypeptides**, polynucleotides, antibodies and/or T cells **may be incorporated** into pharmaceutical compositions **or vaccines**. Alternatively, a pharmaceutical composition may comprise an antigen-presenting cell (*e.g.*, a dendritic cell) transfected with a WT1 polynucleotide such that the antigen presenting cell expresses a WT1 polypeptide. Pharmaceutical compositions comprise one or more such compounds or cells and a physiologically acceptable carrier or excipient. **Certain vaccines may comprise** one or more such compounds or cells and **a non-specific immune response enhancer**, such as an adjuvant or a liposome (into which the compound is incorporated). (emphasis added)

Applicants submit that the skilled artisan would readily appreciate in light of this description that pharmaceutical compositions and vaccines are merely illustrative compositions comprising WT1 of the present invention. Therefore, Applicants submit that the skilled artisan would understand that Applicants were indeed in possession of the claimed compositions comprising non-specific immune response enhancers. Accordingly, Applicants respectfully submit that the instantly claimed subject matter does not constitute new matter and respectfully request that the rejection be withdrawn.

Rejection under 35 U.S.C. § 112, first paragraph (enablement)

Claim 107 stands rejected under 35 U.S.C. § 112, first paragraph as allegedly lacking enablement. In particular, the Action contends that the specification does not disclose how to use the instant invention for the treatment of cancer *in vivo* in humans.

Applicants respectfully traverse this rejection and submit that in *In re Brana*, the Federal Circuit emphatically rejected the PTO position that human clinical testing is necessary to establish practical utility for an antitumor agent. 51 F.3d 1560. Importantly, the court noted, citing *In re Krimmel*, 130 U.S.P.Q. 205 (C.C.P.A. 1961):

> We hold as we do because it is our firm conviction that one who has taught the public that a compound exhibits some desirable pharmaceutical property in a standard experimental animal has made a significant and useful contribution to the art, **even though it may eventually appear that the compound is without value in the treatment of humans**. (Emphasis added)

In the instant application, Applicants have demonstrated *in vivo* that WT1 can be used to induce immune responses (including T helper, antibody and cytotoxic T cell responses) against WT1 and cells expressing WT1 (see Example 3 at pages 44-45, Example 4 at pages 46 and 96, and Example 5 at page 97); whether the compositions will eventually have commercial value in the treatment of humans is not a relevant inquiry in determining patentability.

In further support of the contention that the claims are not enabled, the Action cites Boon, Int. J. Cancer, 54:177-180 1993, allegedly disclosing problems with using tumor derived peptides to treat human cancer. Applicants note that while this reference discusses some potential pitfalls of tumor antigen vaccines, the author, himself a leader in the field of tumor antigen discovery and tumor vaccine development, expresses optimism about the benefit of specific immunotherapy resulting from tumor antigen vaccines (see, in particular, last paragraph of the article). In this regard, to date there are dozens of studies in the U.S., and many more around the world, that involve the use of tumor vaccines, including later studies by Thierry Boon. See for example, PNAS 98:10290-5 where the authors state in the abstract "Vaccination of melanoma patients with tumor-specific antigens recognized by cytolytic T lymphocytes produces significant tumor regressions in a minority of patients. ... Even though [our results] provide no information about the effector mechanisms responsible for the observed reduction in tumor mass

in this patient, they would suggest that low-level CTL responses can initiate tumor rejection." It is wholly unfair to focus solely upon the technical hurdles faced by those in the field while ignoring the successes.

For example, Applicants draw the Examiner's attention to the results of Rosenberg, *et al.*, (1998, Nature Medicine, 4(3):321-327). In this study the authors show that peripheral blood mononuclear cells obtained from patients after immunization with a modified melanoma peptide, but not before, exhibited a high degree of reactivity against the native melanoma peptide as well as against melanoma-positive cells. The administration of the peptide, along with adjuvant IL-2, mediated tumor regression in 42% of patients with metastatic melanoma.

Accordingly, as tumor vaccines as a whole clearly evidence enablement and as Applicants have demonstrated success *in vivo* with generating immune responses to the currently claimed compositions comprising an immunogenic portion of WT1, Applicants respectfully submit that the rejection of the claims under 35 U.S.C. § 112, first paragraph, has been obviated and request that the Examiner withdraw this ground of rejection.

Rejection under 35 U.S.C. § 112, second paragraph (indefiniteness)

Claims 105, 109, 111, and 112 stand rejected under 35 U.S.C. § 112, second paragraph as allegedly being indefinite. In particular, the Action contends that claim 105 lacks antecedent basis for the recitation of "react with WT1 specific antisera" and claims 109 and 111 lack antecedent basis in the recitation of "immune response enhancer" because the claims which they depend from recite "non-specific immune response enhancer".

Without acquiescing to the Examiner's rejection, Applicants have canceled claim 105 without prejudice and have amended claims 109 and 111 to recite "non-specific" immune response enhancer." Applicants submit that the above amendments obviate the rejection and respectfully request its withdrawal.

The Commissioner is authorized to charge any additional fees due by way of this Amendment, or credit any overpayment, to our Deposit Account No. 19-1090.

All of the claims remaining in the application are now believed to be in condition for allowance. Favorable consideration and a Notice of Allowance are earnestly solicited.

Respectfully submitted,

SEED Intellectual Property Law Group PLLC

Julie A. Urvater, Ph.D., Patent Agent
Registration No. 50,461

JAU:tt

Enclosure:
Postcard

701 Fifth Avenue, Suite 6300
Seattle, Washington 98104-7092
Phone: (206) 622-4900
Fax: (206) 682-6031

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